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#JPM24

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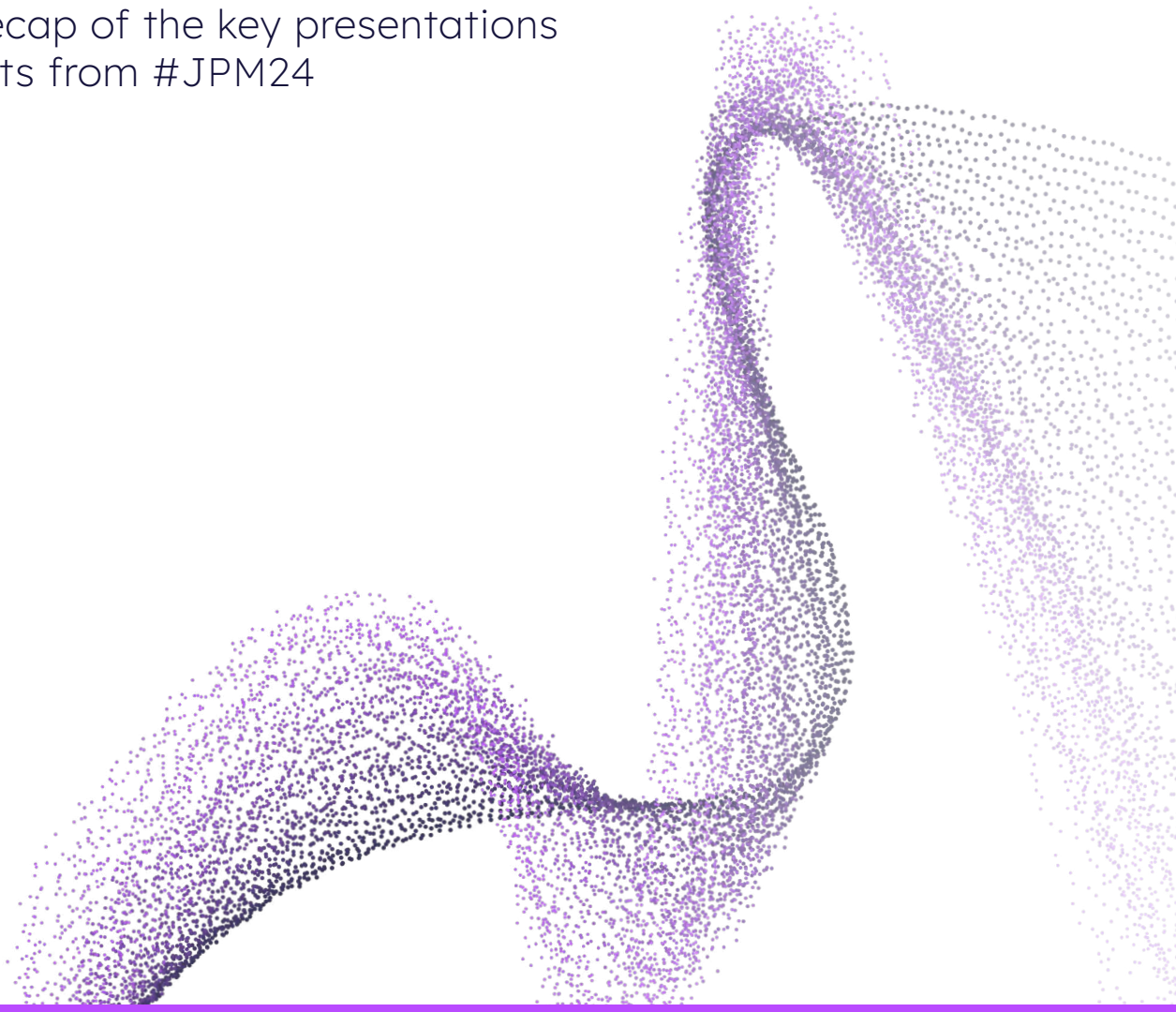
Day 3
Presentations Highlights

A detailed recap of the key presentations and highlights from #JPM24



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Summary

The 42nd annual J.P. Morgan Healthcare Conference (JPM) is being held in San Francisco, CA over 8–11 January 2024. This report contains presentation highlights from a selection of companies from Day 3 of the conference. A complete list of events and catalysts that were announced or updated today is included as a supplement to the report.

About the Author

Biomedtracker is an independent research service that offers proprietary clinical assessments and patient-based revenue forecasts of developmental drugs within a comprehensive and intuitive drug information database. Clients from the pharmaceutical, biotech, and investment industries rely on Biomedtracker for its insight on the likelihood of approval, commercial potential, and future data and regulatory catalysts for drugs within the competitive landscape of every important disease and indication. Over the last several years, Biomedtracker has become the leader in providing objective information alongside evidence-based clinical assessments and investment research on pipeline drugs worldwide. For more information on getting direct access to Biomedtracker, please email clientservices@citeline.com.

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Table of Contents

Mega Cap

AbbVie

At the 42nd annual J.P. Morgan Healthcare conference, president and COO Rob Michael accompanied by the CCO Jeff Stewart and CMO Roopal Thakkar, started off their fire-side chat with a victory lap, highlighting 2023 to be a strong year in growth across their five key therapeutic areas, including read-outs from lead products Skyrivi and Rinvoq. Michael expects continued strong share gains seen for both Sykrivi and Rinvoq over 2024, attributing the anticipated momentum to be driven by fundamental commercial execution coupled with several key catalysts. The company's referral to fundamental commercial execution is pillared in light of the news this week that Skyrizi and Rinvoq secured the top two leading spots in pharmaceutical direct-to-consumer spending, with a collective of over $700 million spent on TV advertisement throughout 2023, holding a testament to Abbvie's investment into their commercial execution. Key catalysts expected for the two powerhouse products include readouts from an unprecedented nine head-to-head trials across indications, alongside a 4th indication approval anticipated midway through 2024. Abbvie's president specifically celebrates the drugs' dominance in the Chron's disease market, with Skyrizi and Rinvoq capturing a third of patients in this market.

As Abbvie's second largest therapeutic area, Michael also anticipates significant growth across their neuroscience platform. The approval of Vraylar in adjunctive major depressive disorder has stood as a strong growth driver for the company, and shares are expected to accelerate in the upcoming year. The oral CGRP receptor anatagonist Qulipta has also seen promising growth and the company plans to see expansion of this drug into international markets in 2024. The Abbvie panel champions a major year ahead for their neuroscience portfolio, expecting growth of over a billion dollars in 2024.

The panel then touched on the aesthetics market and the recovery which it has seen in 2023. They detail how the toxins market is typically at a couple quarter lag but is now recovering, with Abbvie's share position being stronger than before, with the company seeing share gains. This is mostly driven by the launch of new toxin products, such as Volux and Skinvive. It was highlighted that the aesthetics market is seeing a trend to return to growth in 2024, and the company affirms toxins are following this trend, with two quarters of growth. In particular, the company cites their confidence with their share performance, exemplified with their retention of shares in the Botox market despite the launch of Daxxify.

As for the eyecare market, Abbvie recognises the longstanding stability of the market but anticipates a large transform to the pipeline with their Regenxbio partnership, believing the partnered gene therapy to be potentially highly transformative in wet AMD and diabetic retinopathy. The panel continues to underline the attractiveness of the market, stating the easy commercial access to the top physicians.

The presenters also touch on two important deals underway for the company and expresses that

these were designed to provide growth in the next following decade, reiterating Abbvie's confidence with their position and momentum in the current decade. The strategy going forward for these deals will be a focus of the management team to close deals, integrate properly and begin the execution of immigration. They stressed Abbvie's plan for organisational focus on the closure of these deals, with attention channelling towards a smooth transition and integration of these new deals.

In concluding remarks, Michael and the team look forward to another year of strong growth across all therapeutic areas and believe their robust growth platform will help manage anticipated dilution from Humira biosimilar erosion. Abbvie enter 2024 in an optimistic position, with several key global catalysts anticipated.

Large Cap

Genmab

In his JPM 2024 opening remarks, Genmab's CEO Jan van den Winkel reiterated his company's focus to evolve into a "fully integrated biotech innovation powerhouse", focussing on improving the lives of patients through "innovative and differentiated antibody therapeutics". The company's vision is that by 2030, their antibody drugs will transform the lives of cancer patients.

In addition to its eight approved drugs, which are either fully-owned or are owned by third parties but were created by Genmab or incorporate Genmab's innovation—Tivdak, Darzalex, Rybrevant, Kesimpta, Tepezza, Tecvayli, Epkinly, and Talvey—the company also boasts an innovative clinical pipeline, with eleven agents in Phase II and III trials, as well as early clinical development. The eight approved drugs are expected to yield $2.3-$2.4 bn in 2023 revenue, which will sustain the company's efforts to further develop and expand its pipeline.

Co-developed with AbbVie, bispecific antibody Epkinly/Tepkinly, is now approved in the US, Europe and Japan for relapsed/refractory (R/R) DLBCL, and with a subcutaneous delivery that distinguishes it from its bispecific competitors, is considered a great addition to the treatment armamentarium. Following the drug's accelerated approval in the US, Genmab is now pushing Epkinly's development plan further, with five Phase III trials across two indications (DLBCL and FL), in both the front-line setting (which, with a larger target population, is more lucrative than the third-line DLBCL, the drug's current label) and the R/R setting. Genmab is also expanding the drug's early phase development to other indications beyond DLBCL and FL, with CLL and B-cell NHL included in their trials.

Tivdak, the first fully owned Genmab product to receive regulatory approval (In September 2021), is also the first and only antibody-drug conjugate FDA-approved under the accelerated program for second-line recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. In a bid to expand Tidvak's commercial outlook, Genmab is pursuing a broadening of its label to include early lines of cervical cancer, as well as other solid tumors.

Additionally, through its collaboration with BioNTech, Biogen is hoping to further the development of bispecific checkpoint immunotherapy acasunlimab (DuoBody-PD-L1x4-1BB,

currently in Phase II development in NSCLC and endometrial cancer), bispecific immunotherapy GEN1042 (DuoBody-CD40x4-1BB, currently in a Phase I/II trial in solid tumors), and GEN1053 (HexaBody-CD27), a HexaBody technology with potential in solid tumors.

In an attempt to add to their Darzalex franchise, Genmab is also developing the fully-owned investigational agent GEN3014, a HexaBody technology that, like Darzalex, targets CD38 and has shown promising data in preclinical models for multiple myeloma, DLBCL and AML. Developed under exclusive worldwide license and option agreement with Janssen, the drug is being assessed head-to-head with Darzalex in a Phase I/II trial in R/R multiple myeloma and R/R AML. The drug's very high affinity for CD38 may lead to significant efficacy, but it may also be a negative, as its ability to kill CD38-positive cells more potently may also be associated with significant toxicity. This may indeed be problematic, as CD38 expression is found on a variety of cells including on cardiomyocytes.

In closing, van den Winkel indicated that the company's revenue for 2023 is expected to be between $2.3- 2.4 bn, and with Darzalex net sales of $9.8-10 bn, the company expects an operating profit expected to reach between $706-846 million.

Mid Cap

Alkermes

Richard Pops, Chief Executive Officer of Alkermes (ALKS), started the presentation by highlighting the accomplishments of 2023 that led to Alkermes' position as a profitable, pure-play neuroscience company in 2024. Key achievements include the completed separation of the oncology business which streamlined the operational structure and laid the groundwork to expand neuroscience drug development. Patent litigation over VIVITROL was resolved favorably, and financial expectations were raised when the company prevailed in arbitration with Janssen resulting in additional cash flow and a strong balance sheet. The proprietary commercial product portfolio grew in net sales by 20% year-over-year.

One of Alkermes' strategic priorities for 2024 is to deliver strong commercial growth and profitability. This is driven by 4 core products that demonstrate strong, consistent growth generating >$1B: LYBALVI (oral, once-daily treatment option for schizophrenia and bipolar I disorder), ARISTADA (long-acting injectable (LAI) for the treatment of schizophrenia), VIVITROL (LAI for the treatment of alcohol dependence and opioid dependence) and VUMERITY (novel oral fumarate for the treatment of relapsing forms of multiple sclerosis).

Alkermes will leverage its neuroscience drug development capabilities this year to advance its investigational orexin 2 receptor agonist ALKS 2680 for the treatment of narcolepsy. The Phase 1b proof-of-concept study is underway and top line results of the first-in-human study were presented at the 2023 World Sleep Meeting October 2023. Results show strong efficacy and safety/tolerability, and the company plans Phase 2 Narcolepsy Type 1 study initiation in the first half of 2024. The Phase 1b Narcolepsy Type 2 and Idiopathic Hypersomnia proof-of-concept data are also expected during the H1 as well. Alkermes plans to advance other internal development

candidates in psychiatry and neurology and will explore external pipeline opportunities as well.

Alkermes is entering 2024 on a strong foundation for growth. The company is starting the year with ~$800M in cash and investments, while separating its oncology business will result in significant R&D expense savings. The company is planning for significant cash generation from the continued revenue growth from its core commercial products and is expected to be operating cost neutral in 2024.

Amphastar Pharmaceuticals

Amphastar, a bio-pharmaceutical company that develops, manufactures and markets technically challenging generic and proprietary products, presented the company overview and outlook at the 42nd Annual J.P. Morgan Healthcare Conference. CEO Dr. Jack Zhang started the presentation highlighting the fundamental factors that have led the company to success. Firstly, Amphastar has a fully integrated 'One-Stop' business model that allows for the control over quality and compliance at each stage of the product cycle, from R&D to manufacturing and marketing. Secondly, the company adopts a dual-strategies growth model of in-house pipeline development and strategic acquisitions. Lastly, Amphastar follows a 3-H principle; insist on High Quality, emphasize High Efficiency and rely on High technology to develop pipelines. By adopting all of the above, their portfolio of market ready drugs has expanded over the years leading to the diversification of their revenue base and high net income margins.

CFO Bill Peters continued the presentation covering pipeline and product updates. BAQSIMI, Primatene MIST, and Amphastar's generic Glucagon Injection Kit are expected to be their key growth drivers in 2024. BAQSIMI, a novel intranasal glucagon product with IP protection, is a category leader in ease of use due to being the only non-injection glucagon approved by the FDA. The American Diabetes Association (ADA) recommends that patients at increased risk for Level 2 hypoglycemia be prescribed glucagon. Approximately 7 million people are treated with insulin and only about 0.7 million (~10%) of these patients currently utilize glucagon, showing the growth potential of the product. Primatene MIST, a proprietary and patent-protected over-the counter epinephrine inhalation product, was launched in December 2018 and continues to demonstrate its popularity with patients, accounting for 17% of Amphastar sales in 2022. The company is expecting to continue the success of these products in 2024 through the implementation of advertising campaigns and promotions.

In terms of their development pipeline, Amphastar anticipates a number of R&D milestones to occur within 2024. In addition to two recently submitted regulatory filings, the company is expecting three new approvals in AMP-002, AMP-008 and AMP-015 (Teriparatide) and four new regulatory filings later this year. The news is not expected to slow down beyond 2024, as the company is placing a greater focus on developing proprietary and biosimilar products. Their 2025 pipeline is expected to comprise of 50% proprietary, 35% biosimilar and 15% generic compared to 21%, 16% and 63% in 2021 respectively. With a solid financial foundation and diverse pipeline, Amphastar will be looking forward to future news and expanding their market ready portfolio.

Madrigal Pharmaceuticals

Following the NDA acceptance granting priority review in September 2023 for its primary asset resmetirom, an oral thyroid hormone receptor-beta agonist, Madrigal Pharmaceuticals is on track to shift into a commercial pharmaceutical company. Bill Sibold, the newly appointed CEO, focused his presentation on the upcoming PDUFA decision in non-alcoholic steatohepatitis (NASH) for resmetirom in March 2024 and how the company has prepared for its commercialization.

The presentation kicked off with a personal story from a patient advocate. The story highlighted the significant unmet need of NASH and its heavy burden on healthcare systems, accentuated by a lack of disease awareness and therapeutic options. Sibold highlighted that the opportunity to position Madrigal as the leading biopharmaceutical company in NASH will be driven by resmetirom becoming the first foundational therapy for NASH with significant fibrosis. He then stressed that Madrigal is ready to achieve this goal, promising to capitalize the first-to-market status of resmetirom to ensure an effective specialty launch, supported by an experienced commercial team and backed by robust clinical data.

Looking at the clinical data, Sibold again noted resmetirom's profound effects on both key endpoints of interest to regulators: (i) one-stage improvement in fibrosis without worsening of NASH and (ii) NASH resolution without worsening of fibrosis. In addition, resmetirom also demonstrated meaningful improvements on non-invasive fibrosis biomarkers and lipid measures. Rounding out the discussion, Sibold emphasized the favorable safety profile of resmetirom. Most discontinuations were GI-related (diarrhea, characterized as loose stools), but limited to the first 12 weeks. Overall, resmetirom showed a satisfactory safety profile, fitting its position as a chronic therapy.

Looking forward, Madrigal is expecting to rapidly launch resmetirom upon approval in 2024. Sibold hopes to draw from his personal experience launching Dupixent to establish a path from diagnosis to fulfillment for resmetirom, ultimately securing clear market access. Commenting further on the launch execution, Sibold noted that the company will initially target hepatologists and gastroenterologists. Importantly, liver biopsy is not seen as an access barrier. Pricing, however, will be an ongoing crucial discussion with payers ahead of launch. Beyond 2024, Madrigal also hopes to achieve full approval for resmetirom and to secure additional label expansion in compensated cirrhosis patients.

Shockwave Pharmaceuticals

Shockwave Medical's chief executive officer Doug Godshall described the progress of the company during 2023 and the outlook for 2024 and beyond. Shockwave is a medical technology company that produces intravascular lithotripsy (IVL) catheters which modify calcium through a specific form of sonic pressure waves. These catheters are used to target complex calcified anatomies, while minimizing complications, and the company considers the technology to be simple to use which allows it to be easily integrated into clinical procedures.

Godshall enthusiastically described the company's current portfolio which currently has three

catheter products (Shockwave L6, Shockwave M5+, Shockwave S4) for use in peripheral arteries and two catheter products (Shockwave C2, Shockwave C2+) for coronary arteries. Since 2017, these IVL catheters are estimated to have treated >400,000 patients worldwide in the past five years. Shockwave's pipeline has also quadrupled between 2021-2023, with 27 development programs currently ongoing in 2023 vs just 7 in 2021. The company has made significant progress in gaining Medicare reimbursement for their products, and in 2023 coronary inpatients were able to receive reimbursement. Reimbursement access is set to be expanded to include coronary physicians in 2024, with the aim of providing reimbursement to coronary outpatients in the future. In terms of the long-term financial outlook of the company, Godshall expects that between 2024-2026 the company will experience a 25% CAGR in revenue growth and receive over $600 million in R&D investment. A key milestone for the company during 2024 will be setting up a new production facility in Costa Rica.

Small Cap

Agios Pharmaceuticals

Agios Pharmaceuticals has reinforced their status as a frontrunner in the field of cellular metabolism treatments for rare diseases by reviewing their advancements from 2023 and outlining their upcoming projects until 2026. Their currently only approved asset, Pyrukynd [mitapivat] for pyruvate kinase deficiency, continues to be the backbone of their pipeline programs, with Agios exploring its usage in sickle cell anemia and thalassemia. Additionally, the existing indication for pyruvate kinase deficiency is anticipated to be broadened to include pediatric usage through the Phase III ACTIVATE trial. The top-line results of this trial are projected to be announced by the end of 2024, with an estimated approval date in 2026. Mitapivat is a pyruvate kinase activator whose mechanism of action increases adenosine triphosphate (ATP) levels, which prevent dehydration and ion loss in sickle red blood cells (RBCs) and decreases 2,3-DPG (2,3 diphosphoglyceric acid), which promotes oxygen unloading, minimizing sickling and hemolysis.

During 2023, the company reported positive topline Phase III ENERGIZE results for a currently underserved population with non-transfusion-dependent (NTD) alpha- or beta-thalassemia. This patient population makes up approximately two thirds of the disease group; however, this segment has been largely neglected by treatment guidelines in favor of the more severe, transfusion-dependent population. Agios Pharmaceuticals has deduced that this translates to >1 million patients worldwide with 18-23 thousand in the US and EU5 (France, Germany, Italy, Spain, UK) alone. Given the fragmented approach and limited availability of specialist treatment choices, individuals with NTD are generally more prone to experiencing long-term consequences that can negatively impact their quality of life, cause organ damage, and lead to early death. The Phase III results presented are very promising, with 42.3% of patients achieving a hemoglobin response (defined as an increase of ≥1 g/dL in average hemoglobin concentrations) as a primary endpoint and improving on two additional secondary endpoints (fatigue and the average change in hemoglobin concentration) versus placebo. This data is expected to be

submitted for a regulatory filing alongside results from the ongoing Phase III ENERGIZE-T study in transfusion-dependent thalassemia patients, which has a readout expected in mid-2024, for potential broad thalassemia label approval in 2025.

The development of mitapivat in sickle cell disease has also progressed, with positive data reported from the Phase II portion of the RISE-UP study and the Phase III portion underway. A data readout from the Phase III part of the study is expected in 2025 for potential approval in 2026. As with its treatment of thalassemia, a dose-dependent statistically significant increase (~50% of patients) in hemoglobin response rate was observed in the mitapivat group compared to placebo. Positive secondary endpoints such as the improvement in vaso-occlusive crises may help with an accelerated US approval, as the FDA has been more hesitant to grant new marketing authorizations with Pfizer's Oxbryta (voxelotor), a hemoglobin S polymerization inhibitor, already on the market.

Meanwhile, Agios' early-stage pipeline remains active with a positive Phase IIa study of AG-946 for lower-risk myelodysplastic syndromes (LR-MDS), an IND filed for a PAH stabilizer for the treatment of phenylketonuria (PKU), and a licensing agreement with Alnylam for novel siRNA targeting TMPRSS6 for the potential treatment of polycythemia vera (PV). The company remains well funded to achieve the ongoing clinical programs until 2026.

Allogene Therapeutics

In his JPM presentation, CEO Dr David Chang outlined a significant shift in Allogene's business priorities. Allogene's allogeneic CAR-T platform will now focus on four priorities: (i) CD19 targeted cemacabtagene ansegedleucel (cema-cel) as first-line consolidation for large B cell lymphoma (LBCL); (ii) cema-cell for relapsed/refractory chronic lymphocytic leukemia (CLL); (iii) ALLO-329 targeting CD19 and CD70 for autoimmune diseases; and (iv) ALLO-316 targeting CD70 for renal cell carcinoma (RCC).

The lead program is cema-cel for first-line LBCL. Cema-cel was previously being developed for third-line or later LBCL but this setting has become saturated. However, the first-line LBCL setting has challenges of its own, namely that the standard of care, R-CHOP or the more recently introduced Polivy-R-CHP, is very effective with ~60% of patients being cured. As such, the strategy for cema-cel will rely on Foresight Diagnostic's minimal residual disease (MRD) assay to identify the 30% of patients who are at high risk for relapse after responding to standard first-line chemotherapy (another 10% of patients are refractory to first-line therapy and go to second-line). Allogene has announced a partnership with Foresight Diagnostics to develop the investigational MRD assay. Dr Chang presented data showing that Foresight's assay (which has a sensitivity of 1 in 106 cells) is an improvement over the currently approved MRD assays (clonoSEQ and CAPP-Seq, which have a sensitivity of 1 in 106 cells, and 1 in 104 cells, respectively) in identifying LBCL patients who will relapse following front-line therapy. In a retrospective study of 93 patients who received curative first-line therapy, the Foresight assay identified 23 patients as MRD-positive at end-of-therapy. For the 21 MRD-positive patients with >1 year follow-up, 86% (18/21) had progression events within three years. In contrast, 99% of patients (69/70) who were MRD-negative at end of therapy remained alive without progression after three years of follow-up.

The ALPHA3 pivotal trial will evaluate cema-cel as consolidation therapy for patients who respond to front-line therapy (with either a complete response or a partial response) but are MRD-positive. Trial enrollment is expected to initiate in mid-2024 and will compare cema-cel to observation. Part one of the trial will evaluate two different lymphodepletion regimens (FCA vs FC) and an interim analysis will evaluate MRD conversion and safety. Once a regimen has been selected, part two of the study is expected to commence in mid-2025. The primary endpoint for part 2 will be event-free survival (EFS) with key secondary endpoints being PFS and OS. The study is expected to accrue 110 patients and the median EFS for the observation arm is expected to be eight months. Allogene estimates that the addressable US market opportunity is ~7,700 patients/year which could translate to a revenue opportunity >$3 bn.

For the CLL opportunity, a Phase Ib trial (ALPHA2) will evaluate cema-cel in second-line patients who progressed on a BTK inhibitor and third-line patients previously treated with both a BTK inhibitor and a BCL2 inhibitor. ALPHA2 is expected to begin enrolling patients in Q1 2024 with a transition to a potentially pivotal Phase II trial planned by year end 2024/H1 2025. Allogene estimates the addressable population as ~2,500 second-line patients/year and ~5,000 third-line or later patients/year for a revenue potential of ~$3 bn.

CD19 directed CAR-T cells target both tumor and normal CD19-expressing B-lymphocytes and B-cell aplasia is a known side effect of CD19 CAR-T therapy. This CAR-T induced B-cell aplasia has been shown to be beneficial to patients with autoimmune diseases such as lupus and lupus nephritis. It is thought that this benefit may be due to CAR-T cell mediated depletion of lymphocytes reseting the immune system. However, the risk tolerance of patients with autoimmune diseases is different than those with cancer. Furthermore, rheumatologists generally lack experience with the chemotherapy that is typically used for lymphodepletion prior to CAR-T infusion. They also lack experience with leukapheresis procedures and cell therapies. One important differentiator of ALLO-329 is that it targets both CD19 and CD70 with the latter expressed on activated T cells. Since ALLO-329 targets both B and T cells, it may enable lymphodepletion with lower doses of chemotherapy or even chemo-free lymphodepletion. The dual targeting of CD19 and CD70 may also allow for the elimination of both pathogenic B and T cells underlying autoimmunity. Finally, the allogeneic nature of ALLO-329 means there is no need for leukapheresis. ALLO-329 is currently in the IND enabling phase with manufacturing and analytic assays underway. Initiation of a Phase I trial is expected in H1 2025 with potential clinical proof-of-concept data in a yet to be disclosed autoimmune indication expected by the end of 2025.

The RCC program has reported encouraging Phase I data for ALLO-316 with a 30% ORR and 100% disease control in ten CD70+ve RCC patients. Targeting CD70 allows targeting of both tumor cells and alloreactive host lymphocytes. The lymphodepleting properties of the CD70 targeted CAR is also thought to contribute to the remarkable allogeneic CAR T cell expansion and persistence seen in the Phase I trial. However, in some patients, this expansion and persistence was accompanied by a hyperinflammatory response. Allogene has developed a diagnostic and treatment algorithm that may mitigate the hyperinflammatory response without compromising CAR T function. This algorithm will be presented in Q2 2024 and will be incorporated into the ongoing Phase I trial in 2024. A pivotal Phase II trial is expected to initiate by the end of 2025. Longer term plans include evaluating ALLO-316 in other CD70+ve solid tumors as well as hematologic indications including LBCL and T cell leukemia/lymphoma.

Alpine Immune Sciences

Alpine is focusing on developing immune therapies for treating autoimmune and inflammatory disease by leveraging its Directed Evolution Platform. In this presentation, CEO Mitchell Gold discussed the clinical progress of the in-house program known as povetacicept (ALPN-303), which is a Fc fusion protein featuring a modified TACI (transmembrane activator, calcium modulator, and cyclophilin ligand interactor) domain that has been engineered to inhibit both BAFF and APRIL. Following the publication of encouraging data in international conferences last year, Gold announced several upcoming clinical advancements set to begin this year.

Povetacicept, a once monthly subcutaneous injection with a small volume, has been positioned by Gold as the leading dual blocker of BAFF/APRIL, surpassing telitacicept and atacicept. Unlike its counterparts, povetacicept is an Fc fusion protein with a modified TACI domain that has exhibited superior inhibition of both BAFF and APRIL signaling, as demonstrated in Alpine's in vitro assay. The Phase I study RUBY-1, conducted on healthy volunteers, confirmed the significant reduction of immunoglobulins by 80mg and 240mg of povetacicept using a Q4W dosing regimen. The ongoing RUBY-3 study focuses on dose escalation and includes patients with glomerulonephritis including proteinuric IgA nephropathy (IgAN), lupus nephritis (LN), or primary membranous nephropathy (pMN). After six months of treatment with 80mg of povetacicept, the IgAN cohort in the RUBY-3 study revealed a 53.5% reduction in urine protein-creatinine ratio (UPCR), which serves as a predictor of renal function and an endpoint for accelerated approval in IgAN. The depth of UPCR reduction is correlated with clinical outcomes and renal benefit. Gold emphasized that this reduction in UPCR represented the most significant reported to date. Four out of five treated patients achieved clinical remission within six months, defined by UPCR less than 0.5g/g, a reduction of ≥ 50% in UPCR from baseline, and stable renal function with ≤ 25% reduction in eGFR from baseline. In this cohort, the disease-specific marker Gd-IgA1 also decreased by 60%. Patients' eGFR, an indicator of renal function, was slightly increased after six-month treatment. Additionally, povetacicept demonstrated the potential for indication expansion to IgE-mediated diseases, as it substantially reduced all immunoglobulin subtypes (IgA, IgE, and IgM) in addition to IgG. Notably, one subject with pMN experienced a 99% reduction in the pathogenic autoantibody anti-PLA2R1 antibody after six months of treatment, highlighting the selectivity of povetacicept in inhibiting pathogenic antibodies while preserving protective IgG antibodies. Povetacicept exhibited good tolerability without any injection site reactions. Based on these promising results, the company plans to advance povetacicept to a Phase III trial for IgAN patients in the second half of 2024.

Alpine is poised for a year of significant catalysts in 2024. The company will continue advancing povetacicept in two diseases, IgAN and systemic lupus erythematosus (SLE). In the first half of the year, topline data for IgAN at 240mg of povetacicept, as well as follow-up data at 80mg, are expected. Longer-term follow-up data for IgAN will be available in the second half of the year. In the second half of 2024, Alpine will not only initiate a pivotal study for IgAN but also commence a Phase II study for SLE using a placebo-controlled, blinded, and randomized design. Additional data from the RUBY-3 basket trial, which includes LN and pMN patients, will provide further insights into the potential of povetacicept in these diseases. Moreover, the RUBY-4 cytopenia basket study, which enrolls patients with immune thrombocytopenia, warm autoimmune hemolytic anemia, or cold agglutinin disease, will shed light on the expansion of indications

beyond IgAN, with initial results expected in the first half of the year. Povetacicept also holds promise for the treatment of neurological diseases such as myasthenia gravis in the future. Following a follow-on offering last November, Alpine is well-positioned with $368M in cash, which will support the company through 2026.

During the Q&A session, Gold reaffirmed the key strengths of povetacicept, including its monthly injection schedule, significant reduction in UPCR within six months, and dual inhibition of BAFF and APRIL. These factors present a potential opportunity for povetacicept to expand its indications beyond IgAN. When questioned about the decision to move directly to a pivotal study for IgAN, Gold emphasized the acceptance and well-established status of UPCR as an endpoint for IgAN approval. He highlighted the correlation between the degree of UPCR reduction and clinical outcomes. Considering the robust UPCR reduction observed in the current data and the successful precedent set by other companies in IgAN studies, Gold expressed confidence in povetacicept's potential for a pivotal study in the treatment of IgAN patients.

Annexon Biosciences

Annexon Biosciences is a late-stage clinical company focusing on diseases of the body, brain, and eye that are mediated by the classical complement inflammatory pathway. All of Annexon’s assets target C1q, effectively blocking this cascade before upstream and downstream processes can drive inflammation. During his presentation, CEO Doug Love outlined three key milestones that the company plans to achieve in 2024 and noted that Annexon is financially poised to support its ambitious roadmap through Q2 of 2026.

The flagship indication for the company is Guillain-Barré Syndrome (GBS), a devastating neurodegenerative autoimmune disease that causes severe disability and has no FDA-approved treatments. The proof-of-concept study showed that, compared to placebo, ANX005 improved muscle strength, reduced a key inflammatory biomarker, NfL, and improved scores on the GBS disability scale. Specifically, 28% of patients showed a 3-point improvement on this 6-point scale, meaning that some patients who came in on a ventilator were able to walk with assistance by week eight of the study. A Phase III trial targeting the most severe GBS patient population is on track for a readout in Q2 2024, however this trial is taking place entirely in Europe due to a regional difference in alternate treatment availability, although the company plans to pursue US approval as well. These topline results will be the first placebo-controlled dataset for GBS in over 40 years. If all goes well, Annexon plans to prepare a BLA submission in the second half of 2024. ANX005 is also being studied in Huntington’s Disease, Amyotrophic Lateral Sclerosis (ALS), and Lupus Nephritis, indications where the classical complement pathway is validated as a disease driver and there exists a high degree of unmet neet.

Another classical complement-mediated disease is geographic atrophy, an ophthalmic disorder resulting in loss of vision. There is one other treatment approved, Syfovre, but this drug was approved based on a surrogate endpoint of reduction in lesion and not on visual function. In a proof-of-concept study, patients were treated with ANX007 in one eye and a sham injection in the other, resulting in the drug-treated eye experiencing a 74% reduction in loss of function. In the end of Phase II meeting with the FDA, they agreed that the primary endpoint for this registrational program would be improvement of visual function, not a surrogate endpoint. The

program consists of two studies, ARCHER II and ARROW. The former will be initiated mid-2024 and is similar to the initial study, where one eye receives a sham injection, and the latter is a head-to-head comparison with Syfovre. Although ANX007 was granted PRIME designation by the EU, the prospective competitor is not yet approved in that region, so unless European approval is granted, the ARROW study will be based entirely in the US.

Finally, Annexon plans to initiate a proof-of-concept study for its third asset, ANX1502, which is an oral compound targeting only the activated version of a C1q transmitter protein. In a recently completed healthy volunteers study, the drug was not only well tolerated but also reduced elevated complement in these subjects. The upcoming trial assessing ANX1502 in cold agglutinin will begin in the first half of 2024 and topline results are anticipated in the second half.

Centessa

Saurabh Saha, Centessa CEO, opened the presentation describing 2023 as a fantastic year for Centessa, with a strong balance sheet, and momentum expected to continue through 2024 with multiple catalysts. Saha then gave a broad overview of their most advanced programs, the SerpinPC hemophilia program, their orexon agonist program with ORX750 being developed for narcolepsy, and their LockBody technology platform with LB101 for solid tumors. He noted that Centessa's pipeline is diverse and uncorrelate, which for them means the failure of one program won't mean the failure for all programs. Saha also gave an overview on deliverables in 2023, most notably clearing their IND for LB101 and initiating their Phase I/II study in solid tumors, receiving Fast Track designation for SerpinPC for Hemophilia B, and initiating dosing in their SerpinPC Hemophilia B registrational study. The company is expecting a readout from part 1 of the Phase II Present-2 study in 2024.

Saha dove into more detail on their SerpinPC hemophilia program and noted that standard of care treatments for hemophilia have not progressed much beyond IV treatments. He described Centessa's candidate as a safe, subcutaneous, and efficacious treatment that has the potential to transform care for Hemophilia B patients, as there is no subcutaneous treatment option for Hemophilia B in the US and there are limited options for hemophilia B with inhibitors. SerpinPC has the potential for first-in-class subcutaneous therapy with a differentiated safety profile for people with Hemophilia B. With its novel mechanism of action, a 96% reduction in median all-bleeds was achieved in their Phase IIa study, with no thrombosis observed. He highlighted that if this candidate makes it through the clinic, it could be a potential multi-billion dollar market opportunity.

Subsequently he focused on their potential best-in-class oral OX2R agonist for the treatment of narcolepsy and other sleep-wake disorders, ORX750, and how it closely mimics function of the endogenous peptide with high potency. He reported increased wakefulness and suppressed cataplexy in NT1 in preclinical studies in mice. The preclinical data support potential expansion into broader sleep-wake disorders including narcolepsy type 2 and idiopathic hypersomnia, which could be another significant market opportunity for Centessa. Clinical proof-of-concept data in healthy volunteers for ORX750 are expected in 2024.

Lastly, Saha described their LockBody technology platform that combines tumor enrichment with activation of effector function and designed as a single agent systemic treatment. Their first

LockBody candidate is LB101, which demonstrated significant tumor regression during in-vivo studies. The safety profile has shown to be well tolerated in non-human primates with LB101 doses up to 50mg/kg. The company is currently dosing subjects in an ongoing Phase I/IIa first-in-human clinical trial of LB101.

Enanta Pharmaceuticals

President and CEO Dr Jay Luly presented the roadmap for 2024 for Enanta Pharmaceutical. The company's aim is to utilize small molecule drug discovery to develop treatments for high unmet needs with focuses on virology and immunology. Ongoing development of several new assets has been made possible by the successful commercialization of Enanta's glecaprevir, which is a component of Mavyret, an antiviral treatment for hepatitis C marketed by AbbVie. Royalties from this partnership equated to $78.2 million in 2023 with a further $200 million generated from sales of approximately 50% of future royalties. As a result, the company has a balance of $370 million heading into 2024.

Virology has been the main area of focus for Enanta and this continues in 2024 with drug candidates in development for treating respiratory syncytial virus (RSV), covid-19, and hepatitis B virus (HBV) infections. Zelicapavir (EDP-938) is a nucleoprotein inhibitor in development for RSV, a disease with no treatment options at present. Promising preclinical data indicating high potency, high barriers to resistance, and the potential for synergy with other mechanisms of action. Moreover, its once-daily dosing and initial clinical data suggest it may offer benefits over the competitors from Ark Bio and Pfizer also in development. Two global Phase 2 trials, one in children and one in high-risk adults, are ongoing with the first data expected in Q3 2024. A second RSV candidate, EDP-323, targets RNA polymerase, and it too has promising preclinical data suggesting high potency, the potential for synergies, and once-daily dosing. Results from a human challenge study are also expected in Q3 2024. With Covid-19 still an ongoing health concern, Enanta's EDP-235, which targets the 3CL protease, has robust preclinical data with high barriers to resistance and once-daily dosing. Data from the Phase 2 trial did not identify any safety concerns and a reduction in symptoms was observed. However, the company is looking for partners to advance this asset further. Similarly, EDP-514, an HBV core inhibitor, has shown promising Phase 1 data but the company believes it will need to be combined with other MOAs to achieve success.

Dr Luly highlighted the natural expansion of Enanta's areas of focus to include immunology based on the overlap between virology and immunology and the need for orally administered treatment alternatives for immunology indications. The company's first foray is into chronic spontaneous urticaria (CSU), a mast cell driven immunological disorder which affects up to 1% of people worldwide at some stage, and manifests as hives, erythema, and itching. Many patients are not controlled on antihistamines, with the use of biologics also limited, equating to a high unmet need for novel therapeutics. Enanta is aiming to develop a tyrosine kinase receptor (KIT) inhibitor owing to the key role KIT plays in regulating mast cell activity. Proof of concept has been demonstrated with a monoclonal antibody targeting KIT and Enanta is evaluating prototypes looking for oral, potent, and selective KIT inhibitors to advance into clinical development. Further news on candidate selection is expected later this year.

Idorsia Pharmaceuticals

Idorsia Pharmaceuticals' CEO, Jean-Paul Clozel, gave a company overview and expectations for the future at the J.P Morgan Healthcare Conference. He noted that on one side, the company has innovative product offerings, while on the other side the company is restrained by limited financing. What Idorsia wants is to create a sustainable organization, which requires scientific innovation and substantial investment.

The current success of Idorsia is largely based on the company's lead product, Quviviq, approved in the U.S., Canada, and the U.K. for the treatment of insomnia. Quviviq has an optimized pharmacokinetic profile, demonstrating fast absorption and an optimal 8-hour half-life without accumulation over time or active metabolites. This results in patients sleeping through the night without experiencing next morning somnolence. Quviviq launched in the U.S. in 2022, and to date over 125K patients have been treated and over 300k prescriptions have been dispensed. The insomnia treatment has also been launched in Italy, Germany, Canada, Switzerland, and Spain. A commercial launch in France is anticipated in the first quarter of 2024.

Following discussions of Quviviq, Jean-Paul discussed the development status of aprocitentan in resistant hypertension. Approval applications for aprocitentan are currently under review by the FDA and EMA, and has the potential to be the first anti-hypertensive therapy in over 30 years which works via a new mechanism of action and new physiological pathway. The FDA has assigned a PDUFA date of March 19, 2024, for the NDA.

Other late-stage pipeline candidates include selatogrel and cenerimod. Selatogrel is a P2Y12 inhibitor under development for the treatment of acute myocardial infarction (AMI). It is intended to be similar to an EpiPen for AMI, with patients self-administering the drug using an autoinjector at the onset of AMI symptoms, slowing or stopping the heart attack. In Phase II data, subcutaneous administration of selatogrel 8 mg and 16 mg significantly inhibited platelet aggregation and demonstrated a rapid onset of action, within 15 minutes, with the height of its effect extending over 4-8 hours depending on the dose. The Phase III SOS-AMI study is currently recruiting globally, with recruitment in China initiating later in 2024.

Cenerimod, an S1P1 receptor modulator, is in development for systemic lupus erythematosus (SLE). Idorsia believes that cenerimod is the ideal treatment for SLE because it prevents the migration of T-cells and B-cells into target organs and prevents the migration of antigen presenting cells and priming of autoreactive lymphocytes. Two Phase III OPUS studies are currently recruiting globally.

Idorsia estimates its current cash reserves to last to early April 2024, and therefore plans to extend the cash runway through various avenues, including potential partnership and out-license deals. In 2024, Idorsia wants to fund the company without selling everything, while retaining shareholder value within.

IGM Biosciences

IGM Biosciences presented at the JPM Healthcare Conference providing updates on its IgM

antibody platforms, collaboration agreement with Sanofi, and financial position as of 2023. The company ended the year with approximately $338 million in cash and investments, with runway expected into the second quarter of 2026. The worldwide research collaboration with Sanofi is expected to develop agonists using IGM's proprietary antibody technology against three oncology targets and three autoimmunity and inflammation targets. Per the terms of the agreement, IGM has received an upfront payment of $150 million from Sanofi, with potentially $6 billion in preclinical, clinical, regulatory, and commercial milestone payments. Sanofi will be responsible for the worldwide commercialization of the IgM agonist product.

IGM's pipeline consists of three products: Aplitabart, Imvotamab, IGM-2644. Aplitabart is a multimeric DR5 agonist currently being investigated in a clinical trial for second line metastatic colorectal cancer, investigating progression free survival as the primary endpoint and objective response rate, overall survival, and safety as secondary endpoints. The company plans to enroll approximately 110 patients in the Phase I trial by the first quarter of 2024. Imvotamab is currently being investigated in systemic lupus erythematosis, rheumatoid arthritis, and idiopathic inflammatory myopathies (myositis). The trials in SLE and RA are currently enrolling and the trial in myositis is expected to initiate in the first quarter of 2024. IGM-2644 is currently in preclinical development for the treatment of autoimmune diseases.

As 2024 progresses, we anticipate IGM's undisclosed product in collaboration with Sanofi to make a worldwide impact. We expect IGM's domestic pipeline to mature with time, with topline data once the patient cohorts have been completely enrolled.

Ironwood Pharmaceuticals

Ironwood CEO Tom McCort began his presentation speaking of the company's vision of becoming the leading GI healthcare company focused on advancing the treatment of GI diseases and redefining the standard of care for those patients.

Linzess is the US prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC). The growth is driven primarily by patients coming over from the OTC space. Linzess is the first and only FDA approved prescription therapy for patients with pediatric functional constipation (PFC) for patients ages 6-17. This is an area with significant unmet need and opportunity. The drug became commercially available for the PFC indication in June 2023. Ironwood has an efficient investment planned to realize its full opportunity.

Apraglutide is a potentially best-in-class glucagon-like peptide 2 (GLP-2) analog for short bowel syndrome for intestinal failure (SBS-IF). It has potential to establish a new standard of care with its once-weekly dosing as opposed to daily dosing like other drugs for the condition. The drug has unique pharmacological properties including long half-life which supports the once-a-week dosing regimen. The STARS Phase III trial is the largest GLP-2 trial ever conducted for the SBS-IF population. Topline date is expected in March 2024. Apraglutide has the potential to achieve $1B in peak net sales.

Ironwood's CNP-104 has the potential to be the first disease-modifying therapy for primary biliary cholangitis (PBC) by targeting the root cause of the disease. There are currently no

therapies on the market to address the root cause of the autoimmune destruction of the bile ducts. Initial assessment provided evidence of favorable T-cell response in patients dosed with CNP-104. Ironwood maintains an option from Cour Pharmaceutical to exclusively license US rights to CNP-104 for continued development pending proof-of-concept and commercial viability. Ironwood expects topline data from the Phase II study in Q3 2024. Through Linzess, apraglutide, and CNP-104, Ironwood can potentially generate revenues of over $1.5 billion through the 2030s.

CEO McCourt closed out his presentation saying that 2024 has the potential to be a transformational year for Ironwood. The company is uniquely positioned to drive value as a GI-focused biotech with multiple 2024 development catalysts and strong Linzess cash flows expected until generic entry in 2029.

Lexeo Therapeutics

Lexeo Therapeutics, a genetic medicine company aiming to bring precision medicine to disease areas with little or no penetration, set out its strategy for 2024 at this year's JPM Healthcare conference. CEO Nolan Townsend outlined the company's vision and development plans, noting that evolving regulatory environments and shifting treatment landscape have yielded untapped potential for his well-positioned company. Lexeo Therapeutics is targeting its gene therapies at areas where it sees its non-viral AAV vector excelling, specifically cardiovascular disease and Alzheimer's disease.

Townsend highlighted the company's pipeline, mainly its Phase I/II stage assets LX2006 and LX1001 under development for Friedreich's Ataxia cardiomyopathy and APOE4-associated Alzheimer's disease, respectively. The company's next most advanced program is its arrhythmogenic cardiomyopathy therapy LNX2020, which is expected to move into clinical studies shortly. With this and LX2006, Lexeo Therapeutics is hoping to be the first company with two cardiovascular gene therapy programs in clinical studies with data readouts expected in 2024. Regarding Lexeo's Alzheimer's program, interim data from all cohorts of the Phase I/II are expected in the second half of 2024, likely at Clinical Trials on Alzheimer's Disease conference (CTAD). Townsend enthusiastically presented the company's plethora of non-clinical and clinical evidence supporting the company's cardiovascular and Alzheimer's pipeline in tandem with comments on aligning development plans such as study designs with regulatory precedents. Rounding off the presentation, Townsend proudly summarized the company's expected catalyst for 2024 and briefly touched on the financial runway extending into the fourth quarter of 2025. In summary, Lexeo Therapeutics utilized its JPM presentation to stake its ambitious claim on under-developed disease areas with its unique AAV technology and strategic pipeline.

Liquidia Corporation

Liquidia has been making progress towards its mission to develop treatments for pulmonary arterial hypertension (PAH). Liquidia's main product, Yutrepia, an inhalation dry powder, achieved tentative approval in 2021 for pulmonary arterial hypertension (PAH) and an additional PDUFA for pulmonary hypertension associated with interstitial lung disease (PH-ILD) is set for January 2024 with no additional clinical trials needed for review. Due to the Hatch-Waxman Act,

Yutrepia for PAH cannot be marketed in the United States, but favorable regulatory standards were reached leading to tentative approval, establishing the safety and efficacy of Yutrepia and Liquidia's PRINT technology. Additionally, final approval wtih PH-ILD cannot occur until the regulatory exclusivity for Tyvaso expires on March 31, 2024.

In relation to the litigations to Yutrepia, Liquidia has stated the company has not found infringement on the claims for the '793 patent asserted by United Therapeutics. Liquidia also declared the '327 patent was not infringed upon and additionally the patent was not submitted to the Orange Book before the original NDA was filed. In January 2024, Liquidia filed the latest response to United Therapeutics under the Hatch Waxman Act to the District Court. Liquidia continued to prepare its sales and commercial team and is ready to launch Yutrepia when given the green light to.

Liqudia is also developing L606 for North America in partnership with Pharmosa, a sustained release Treprostinil, for PAH and PH-ILD. In December 2023, Liquidia held a Type C meeting with the FDA to discuss a registration pathway for L606. A Phase III global placebo-controlled study in PH-ILD is expected to initiate in 2024 to support both PAH and PH-ILD with a safety study continuing to enroll. Liquidia reiterated the company is in position to be well-capitalized through 2024 supported with a $126M financing raised since the third quarter of 2023 to support development goals and the launch of Yutrepia.

Lyell Immunopharma

Lyell Immunopharma (LYEL) CEO Lynn Seely, MD, presented this year's JPM discussion surrounding the company's T-cell therapies in development for cancer. Lyell uses its genetic and epigenetic reprogramming technologies to create CAR-T cells and tumor infiltrating lymphocytes (TIL) that resist exhaustion and have durable stemness (the ability to self-renew).

Lead CAR-T cell candidate LYL797 is in Phase trials for triple-negative breast cancer, non-small cell lung cancer, and other ROR1+ solid tumors. Dr. Seely reviewed preclinical data exhibiting key differentiators (tumor reduction, enhanced cytokine production, and tumor infiltration in aggressive NSCLC syngeneic model with c-Jun CAR T cells) and noted the candidate's efficacy with c-Jun overexpressing ROR1 CAR-T cells in aggressive NSCLC. Ongoing Phase I dose escalation and dose expansion trials are underway in relapsed/refractory TNBC and NSCLC patients who are ROR1 positive, with initial data on about 20 patients expected during the first half of 2024.

In the TIL pipeline, Dr. Seely discussed LYL845, which has exhibited robust TIL expansion across immunologically hot and cold tumors. Developed with the company's Epi-R manufacturing protocol and Stim-R technology, LYL845 produces long-lived effector cells. Phase I trials are underway in melanoma, NSCLC, and colorectal cancer, with initial data readouts planned in the second half of 2024.

Dr. Seely closed by noting that the company has partnered with Cellares and its automated manufacturing processes that can produce up to 800 doses of LYL797 per year. For other projects, Lyell produces its Phase I clinical supply in-house at the LyFE manufacturing center.

Novocure

Novocure are a company focused on developing Tumor Treating Fields technology, or TTFields technology, which uses electric fields to disrupt cell division causing cancer cell death; Novocure are planning on using this technology via their Optune medical device to target the most aggressive forms of cancer. The Executive Chairman Bill Doyle started the presentation by highlighting the three key pillars of their strategy for long-term growth: driving commercial adoption, advancing clinical trials, and delivering product innovation.

Doyle reported that Optune has generated over $500mn in net revenue, with over 3,750 patients being treated with this technology. Importantly the NCCN, have given Optune their highest possible recommendation in glioblastoma, a category 1, based on excellent OS data seen in the Phase 3 EF-14 trial, which is vital in advancing physician trust and familiarity. This is particularly notable as glioblastoma is a notoriously difficult cancer to treat. However, Novocure has only achieved 30-40% penetration in key countries, a statistic they aim to improve going forward.

The TTFields technology has also had positive data in the Phase 3 LUNAR trial in metastatic NSCLC patients with no mutational biomarkers who have progressed on platinum chemotherapies in the first-line; an area of huge unmet need. Novocure estimate ~30,000 patients will seek second-line therapy in this setting, a large population which could generate significant profit. Based on this trial, Novocure hope to launch Optune in NSCLC in 2025, with the expectation of submitting Phase 3 data to the US and Japan in 2024.

Novocure are also investigating Optune in patients following SRS therapy for brain metastases from NSCLC and in pancreatic cancer patients, with Phase 3 readouts expected in both these indications in 2024. Positive data could allow access to large patient populations in areas of high unmet need, creating a large amount of opportunity for Novocure. In the earlier stages of development, they are looking at Optune efficacy in glioblastoma multiforme (GBM), and in various combinations and settings in both NSCLC and pancreatic cancer.

Doyle concluded by addressing the announcement that Novocure had undertaken a structural reorganization at the start of 2023, wherein ~200 employees were let go, stating they needed to "remove some of the fat" in order to maximize profits and allow focused innovation. As a smaller pharma company, developing relationships with governments, securing reimbursement for Optune, upscaling production to meet demand, and educating HCPs and patients on the benefits of Optune to promote uptake will be essential factors affecting Novocure's growth.

Pacira BioSciences

Frank D. Lee, who has been CEO at Pacira BioSciences for only a week, started the presentation by explaining how he was compelled to join the company following a year of semi-retirement. He was impressed by the company's leading presence in the non-opioid pain management space, via three of its assets; Exparel, Zilretta, and iovera. Exparel is an expensive injectable formulation of bupivacaine, and is the only long-acting, local and regional analgesic with a broad approval for postsurgical pain. Zilretta is the only FDA-approved extended-release intra-articular

injection for osteoarthritis knee pain, and iovera is the only novel, handheld device for immediate, long-lasting, drug-free pain control using advanced cold technology.

In 2023, the FDA approved a supplemental new drug application for the use of Exparel in lower extremity procedures as an adductor canal block and a sciatic nerve block in the popliteal fossa, following strong clinical data versus an active comparator. With more than three million lower extremity procedures taking place annually, Pacira has forecasted annual sales of $100 million+ within five years.

Pacira claims to have a strong financial and operational foundation to self-find growth. At the end of 2023, the company had $280 million on its balance sheet, with total net product sales of $669.9 million, with $538.1 of these sales attributable to Exparel. Additionally, Pacira reported an adjusted EBITDA of at least $210 million for 2023, which is slightly lower than the $212.7 million reported for 2022.

Pacira will directly benefit from the "Non-Opioids Prevent Addiction in the Nation" or "NOPAIN" act, which was signed into law in December 2022 and takes effect in January 2025. The NOPAIN act directs the Centers for Medicare and Medicaid Services (CMS) to reimburse non-opioid and opioid treatment separately across all outpatient settings, in hopes of reducing or replacing opioid consumption. This should help to reduce the pressure on providers to prescribe opioids by ensuring that approved non-opioid options are more widely available to individuals as a post-surgical treatment option. There are currently six branded pharmaceuticals with FDA approvals for post-surgical pain that will benefit from the NOPAIN legislation. Pacira expects the NOPAIN act to drive Exparel sales to over $1 billion. Lee emphasized the importance of educating customers and stakeholders about NOPAIN and how it will impact them.

Currently, Pacira is focusing on growth and expanding its contract base with group purchasing organizations (GPOs). New GPO partnerships are expected to be launched in 2024. This should expand access and make non-opioid pain management more broadly accessible in inpatient settings, whereby ~25% of Exparel-relevant market procedures take place.

RAPT Therapeutics

Pipeline-stage Rapt Therapeutics dedicated their platform at the JPM conference to detailing results from their two oral small molecule drugs, zelnecirnon and tivumecirnon, being developed in inflammation and oncology, respectively. As these represent very different areas, the company plans to focus on zelnecirnon and is in active discussion with several parties about the potential to partner on the oncology asset, tivumecirnon.

The company's lead inflammation asset, zelnecirnon, is a once daily oral agent that targets inflammatory Th2 cells. Framing this as a potential pipeline-in-a-product, the CEO Brian Wong compared the asset to anti-IL4 antibody, Dupixent, which is approved in several inflammatory indications and touted the drug as having disease-modifying potential due to its upstream mechanism of action. In a Phase Ib atopic dermatitis study, the novel CCR4 antagonist showed safety consistent with the lack of a need for laboratory monitoring, or black box warning, similar to oral Otezla. At day 29, zelnecirnon achieved a 33% placebo-adjusted rate of EASI-50 which increased to a 42% difference 2-weeks after patients stopped the one-month treatment. Brian

Wong used the OX40 class as an analog for the potential disease altering success, zelnecirnon blocks the binding of CCL17 and CCL22 to CCR4 thereby inhibiting the trafficking of Th2 cell migration into lesional skin and reducing inflammatory cytokines, like IL-4. However, data on the primary endpoint for an oral drug in atopic dermatitis was lower, with 14% of treated patients achieving an IGA of clear or almost clear, though this still compared to no patients on placebo. The primary endpoint for the Phase IIb study is EASI, but the placebo difference in IGA, measured as a secondary outcome in this ongoing study, will be of interest. Regardless, with potential for better efficacy than Otezla, Rapt CEO highlighted that zelnecironon could be positioned as the first choice after an inadequate response to topical cortical steroids, but prior to injectables or oral JAK inhibitors. A Phase IIb study is enrolling, with data expected mid-2024, which could set up Phase III studies to start in 2025, if successful.

Additionally, the company started a Phase IIa proof-of-concept study in asthma, with a design that initially evaluates the drug as an add-on to inhaled medications but, after a just over a month, follows a tapering to monotherapy use for the last three weeks. The company is also looking to explore the use of zelnecirnon in type 2 COPD.

Rapt is evalauting CCR4 antagonist, tivumecirnon, in oncology by selectively inhibit regulatory T cell trafficking specifically into the tumor but not into healthy tissues. The drug has been evaluated in proof-of-concept studies as a monotherapy, but also in combination with pembrolizumab, with a 45% objective response rate in patients with checkpoint naive non-small cell lung cancer. A South Korean study run by Hanmi showed a 67% response rate in EBV positive gastric cancer.

Vericel

Vericel CEO (Chief Executive Officer), Nick Colangelo kicked off the presentation by highlighting the company's lead product, MACI – an advanced cell therapy that rebuilds damaged cartilage and function using the patient's own cells. Colangelo was keen to note that MACI has become the leading cartilage repair product in the sports medicine market, and it is the only FDA (Food and Drug Administration) approved product of its kind.

Moving into the burn care market – another important focus for Vericel, the presentation focused on the recent U.S (United States). product launch of NexoBrid. This product, which is indicated for the removal of eschar in adult patients is another product by the company which is the only FDA approved permanent skin replacement treatment for burns on patients with greater than 30% total surface area burns.

There is currently no established biosimilar, generic or 510(k) pathway for products like MACI or Epicel. This is due to the products having a biological competent that work with the patient's own cells which ultimately means these products are regulated by the FDA. Due to this regulation, it makes it difficult for a competitor to compete in these therapeutic spaces as they would have to run a full clinical development program. Additionally, the approval of NexoBrid came with an orphan designation which results in orphan market exclusivity in the U.S. and the product has patent protection into the 2030s. With all this combined, Colangelo was eager to point out the high barriers of entry present for potential competitors looking to encroach on Vericel's market share.

This market exclusivity has also led the company to have a solid financial profile – delivering positive adjusted earnings and operating cash flow every quarter for the last 3.5 years – with the company ending the year with $152 million in cash and no debt.

Looking to the future, Vericel are keen on advancing their pipeline with two regulatory submissions in the fourth quarter of 2023. Firstly, the supplemental BLA (Biologics License Application) submission for NexoBrid in a paediatric indication and secondly, the submission for MACI arthroscopic delivery. Both submissions have been accepted for review by the FDA.

With a high revenue growth profile, sustained positive operating cash flow and around $152 million in cash and investments, the company is financially very secure. With anticipated regulatory approval decisions and product launches just around the corner the future looks bright for Vericel.

Voyager Therapeutics

Voyager Therapeutics is coming into 2024 with plans to become a clinical stage company once again with 4 INDs expected in 2024 into 2025, with plans to generate data by 2026. At the beginning of 2024, Voyager announced a $100 million IPO along with a new Novartis partnership for its Huntington's disease and spinal muscular atrophy therapies where the company received an additional $100 million up-front payment, including a $20 million equity investment. As such the company has a cash runway in 2027, with an estimated $8.2 billion in potential milestone payments.

The investment and funding were secured based on the potential of its TRACER-derived capsids. Voyager views this as a potential replacement to current AAV9 gene therapy delivery systems, showing a 100-fold improvement over parental capsid tech of AAV9. Voyager is planning to advance VY-TAU01 for Alzheimer's disease with an IND filing in the first half of 2024, a Phase IA single ascending dose study in 2024 and a Phase Ib multiple ascending dose study in 2025. Following this therapy, Voyager is continuing studies to advance its SOD1 silencing gene therapy for the treatment of ALS.

Micro Cap

Kodiak Sciences

Kodiak, a company specializing in ophthalmology medicine has had a relatively quiet H2 2023 focusing on phase studies and excelling in manufacturing. Focusing on breakthrough and innovation, CEO Victor Perlroth started the presentation highlighting the commercial attractiveness of retinal medicine, with Kosiak future focus on three main areas: 1) trailblazing science with a creative foundation, 2) leading in generation 2.0 medicine, and 3) singular focuses on ophthalmology. With a balance sheet on $346 mill cash (Q3 2023,) Kodiak aims to address multiple unmet needs in this therapy area with investments into their diversified pipeline in the next 2-3 years. This includes tarcocimab tedromer, an anti-VEGF therapy already in positive phase 3 studies for diabetic retinopathy (NPDR), retinal vein occlusion (RVO) and wet

AMD, KSI-501, a first-in-class anti-IL-6 and anti-VEGF bispecific therapy designed to treat intraocular inflammation and retinal vascular disease, and finally, an unconjugated bispecific version of KSI-501 developed for retinal inflammatory diseases. A new market analogue from the established anti-VEGF market with plans towards pivotal study initiations in 2024.

Driving initial focus on tarcocimab tedromer, Perlroth highlighted that across the entire clinical program and ABC platform, the drug demonstrated consistent and differentiated durability and favorable safety. Successful pivotal data was observed in NPDR, whereby tarcocimad continued to establish superior efficacy when dosed every 6 months, observing 90% reduction in risk of developing sight-threating complications with a 29x increased response rate within 48 weeks. In RVO, tarcocimab continued to demonstrate strong durability, matching efficacy and comparable safety profile with significantly fewer doses than the marketed anti-VEGF aflibercept (Sanofi) whereby results saw 30% higher chance of patients not requiring additional doses and 46% of patients requiring no additional injection in the second 6 months. Kodiak are planning to initiate an additional pivitol study in H1 2024 (24 months) to support the single BLA application for all three indications with beliefs that tarcocimabs breath of indications, signature durability, combined with appropriate commercial strategy could support physicians' adaptation and translation of the product into the growing anti-VEGF market.

Entering a novel category of retinal medicine, Perlroth continued to draw attention to KSI-501p and uncoupled KSI-501ABC, an anti-VEGF and anti-IL-6 inhibitor to address inflation and its underlying inflammatory cascade. With substantial patient- patient variability observed in the anti-VEGF monotherapy, the need for additional mechanism of action has initiated Kodiak to innovate this dual-inhibition therapy which was shown significant pre-clinical results showing inhibition on angiogenesis and normalization of inner and outer blood retinal barriers. Kodiak are currently exploring initiation of dual phase 2/3 pivitol studies on KSI-501ABC in high prevalence retinal vascular diseases after recent phase 1 study in DME patients in 2023. Plans are also underway for the unconjugated KSI-501p with phase 1/2 expansion studies underway in H1 2024 with topline data expected in the next 2 years.

Rallybio Corporation

Rallybio's Chief Executive Officer, Stephen Uden, began the presentation with an overview of who the company is and how they got to where they are now. Uden shared that Rallybio is a portfolio company looking for therapeutics that will be revolutionary in rare disease research and development. The company believes they are currently in a strong financial position and are consistently building upon their global business development expertise.

Uden then went on to share the company's current pipeline which includes four therapeutics areas: maternal fetal blood disorders, complement dysregulation, hematology, and metabolic disorders. The company currently has two clinical programs in assets RLYB212 and RLYB116, both of which are poised to enter phase two.

Next, Uden gave an overview of RLYB212, the company's potential preventative treatment for fetal and neonatal alloimmune thrombocytopenia (FNAIT). RLYB212 is a fully human monoclonal anti-HPA-1a IgG that was derived from a plasma cell. RLYB212 is currently in phase one development and Rallybio expects to provide an update on phase two discussions with the

European Medicines Agency (EMA) in the first half of 2024. Assuming these discussions go well, the company plans to initiate a phase two dose confirmation study in the second half of 2024. This study is designed to confirm the RLYB212 dose regimen in pregnant women at higher risk of FNAIT prior to initiation of a larger phase three registrational study. Uden also gave an overview of results from the ongoing single-arm, open-label study to assess the pharmacokinetics (PK) and safety of subcutaneously (SC) administered RLYB212 in pregnant women at higher risk for HPA-1a alloimmunization. These data showed that RLYB212 was observed to be well-tolerated with no reports of serious or severe adverse events. RLYB212 produced dose-dependent, rapid and complete elimination of transfused HPA-1a positive platelets, achieving over ninety percent reduction in mean platelet elimination half-life in both dose groups versus placebo.

Uden continues the pipeline updated with discussions on RLYB116 and RLYB114, both of which are advanced inhibitors of C5 that offer high potency, less frequent dosing, and ease of use. RLYB116 is currently in phase one trials in Australia in healthy participants for the treatment of complement deficiencies/abnormalities. RLBY114 is still in the preclinical phase, and we can expect an update on when this asset will enter the clinical space during Rallybio's next portfolio update which will take place in the second half of 2024.

Uden finished the pipeline section of the presentation by briefly highlighting RLYB331, a monoclonal antibody that selectively targets matriptase-2 (MTP-2) serine protease that plays a role in hepcidin formation, and the company's ENPP1 inhibitor which is a joint venture with Exscientia to discover/develop small molecule therapy to treat hypophosphatasia. For RLYB331, preclinical activities are currently underway, and the company expects to report additional animal data in the first half of 2024.

Finishing the presentation, Uden highlighted again the mentioned upcoming milestones for the year as well as a few success drivers the company believes they currently possess that will allow them to succeed in these planned ventures. These success drivers include their diversified portfolio, their proven innovation thus far in research and development, their current robust financial position, and their pursuit of global business development expertise.

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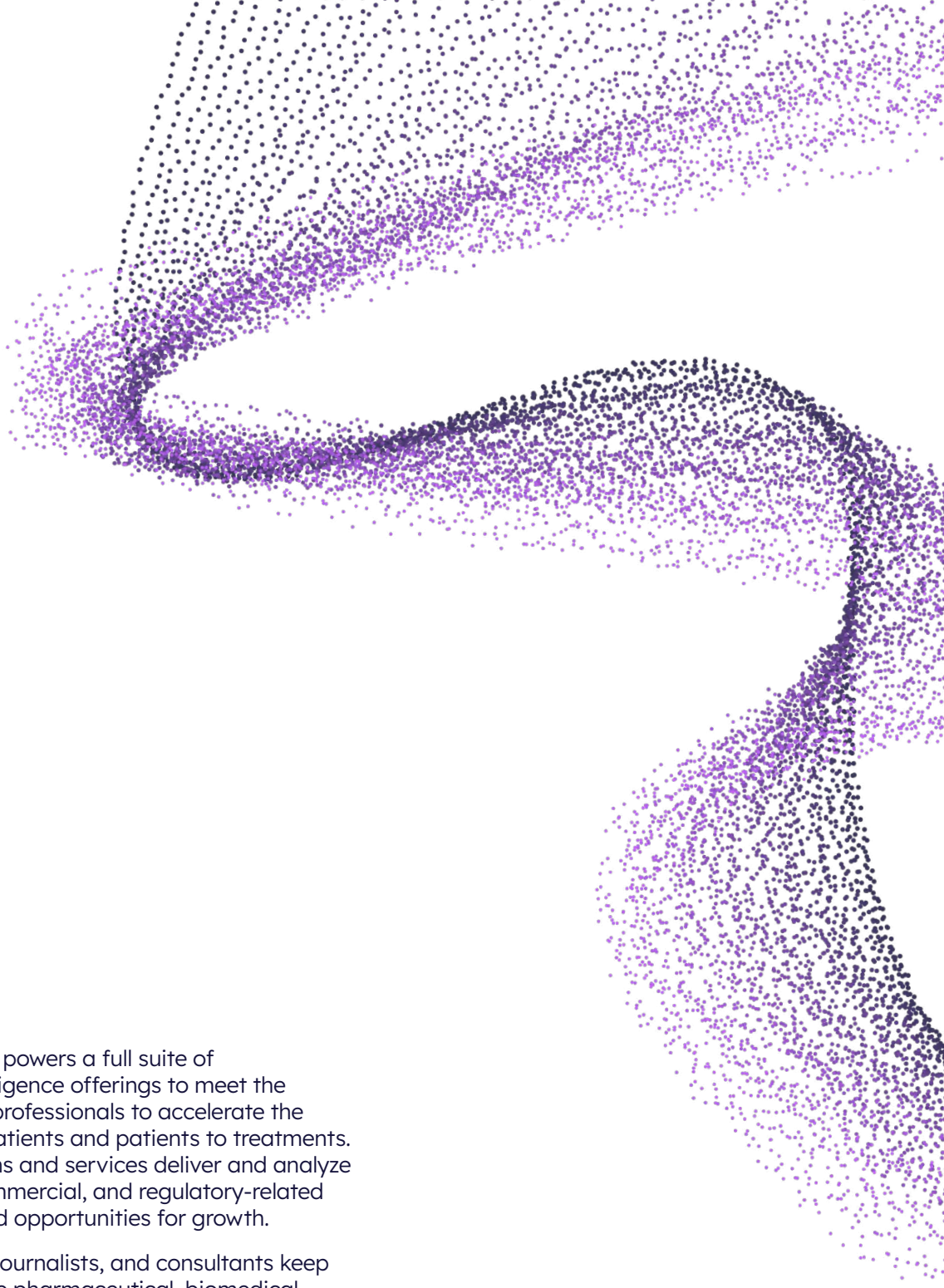

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